137. A method according to any one of claims 133-136 wherein the nucleotide sequence is selected from the group consisting of

(a) a nucleotide sequence encoding the Hu-Asp1 amino acid sequence set forth in SEQ ID NO: 1;

(b) a nucleotide sequence encoding a fragment of Hu-Asp1 (SEQ ID NO:1), wherein said fragment exhibits aspartyl protease activity characteristic of Hu-Asp1

(c) a nucleotide sequence of a polynucleotide that hybridizes under stringent hybridization conditions to a Hu-Asp1-encoding polynucleotide having the sequence set forth in SEQ ID NO: 1.

138. A method according to any one of claims 134-137, wherein the cell comprises a vector that comprises the polynucleotide.

139. A method according to any one of claims 131-138, wherein the APP comprises the Swedish mutation (K→ N, M→ L) adjacent to the β-secretase processing site.

140. A method according to any one of claims 131-139, wherein the APP further comprises a carboxy-terminal di-lysine.

141. A method according to any one of claims 131-140, wherein the test agent is an inhibitor

142. A method according to any one of claims 131-140, wherein the test agent is an agonist.

143. A method according to any one of claims 131-142, further comprising a step of treating Alzheimer's Disease with an agent identified as an modulator of Hu-Asp1 according to steps (a)-(c).

144. The use of an agent identified as an inhibitor of Hu-Asp1 according to any one of claims 131-142 in the manufacture of a medicament for the treatment of Alzheimer's Disease.

145. A method of reducing cellular production of amyloid beta (Aβ ) from amyloid precursor protein (APP), comprising step of transforming or transfecting cells with an anti-sense reagent capable of reducing Asp1 polypeptide production by reducing Asp1 transcription or translation in the

cells, wherein reduced Asp1 polypeptide production in the cells correlates with reduced cellular processing of APP into Aβ .

146. A method of reducing cellular production of amyloid beta (Aβ ) from amyloid precursor protein (APP), comprising steps of:

(a) identifying mammalian cells that produce Aβ ; and

(b) transforming or transfecting the cells with an anti-sense reagent capable of reducing Asp1 polypeptide production by reducing Asp1 transcription or translation in the cells, wherein reduced Asp1 polypeptide production in the cells correlates with reduced cellular processing of APP into Aβ .

147. A method according to claim 146, wherein the identifying step comprises diagnosing Alzheimer's disease, where Alzheimer's disease correlates with the existence of cells that produce Aβ that forms amyloid plaques in the brain.

148. A method according to any one of claims 145-147, wherein the cell is a neural cell.

149. A method according to any one of claims 145-148, wherein the anti-sense reagent comprises an oligonucleotide comprising a single stranded nucleic acid sequence capable of binding to a Hu-Asp1 mRNA.

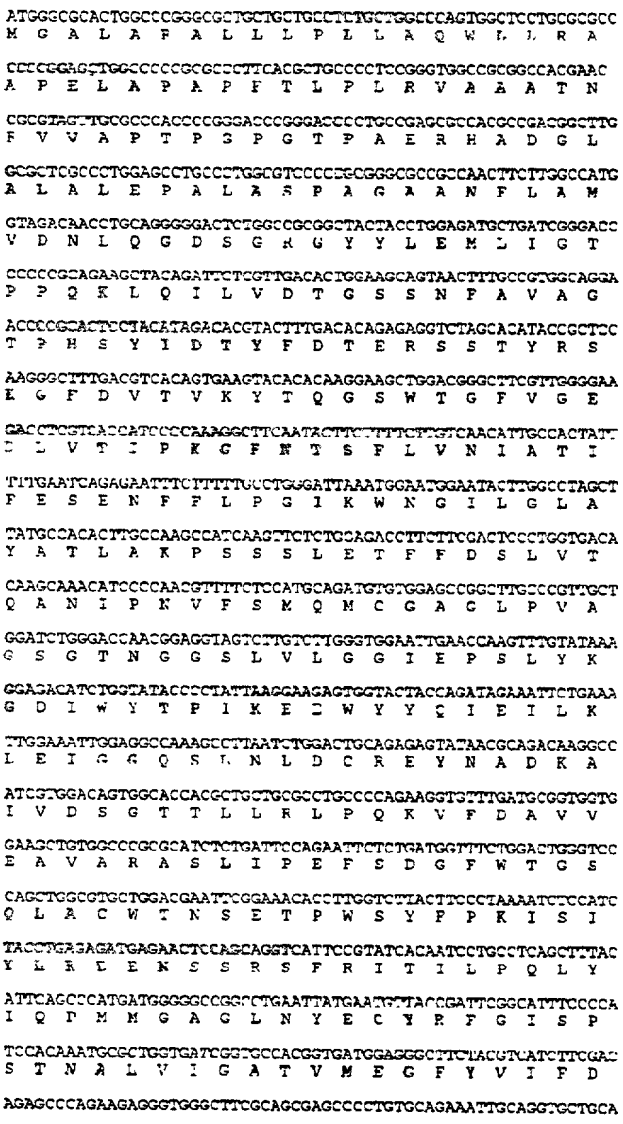
150. A method for the identification of an agent that decreases the activity of a Hu-Asp polypeptide selected from the group consisting of Hu-Asp1, Hu-Asp2(a), and Hu-Asp2(b), the method comprising

(a) determining the activity of said Hu-Asp polypeptide in the presence of a test agent and in the absence of a test agent; and

(b) comparing the activity of said Hu-Asp polypeptide determined in the presence of said test agent to the activity of said Hu-Asp polypeptide determined in the absence of said test agent;

whereby a lower level of activity in the presence of said test agent than in the absence of said test agent indicates that said test agent has decreased the activity of said Hu-Asp polypeptide..

FIGURE 1 (1)


ATGGGCGCACTGGCCCGGGCGCTGCTGCTGCCTCTGCTGGCCCAGTGGCTCCTGCGCGCC
M G A L A R A L L L P L L A Q W L L R A
CCCCGGAGCTGGCCCCCGCGCCCTTCACGCTGCCCCTCCGGGTGGCCGCGGCCACGAAC
A P E L A P A P F T L P L R V A A A T N
CGCGTAGCTGCGCCCACCCCGGGACCCGGGACCCCTGCCGAGCGCCACGCCGACGGCTTG
F V V A P T P S P G T P A E R H A D G L
GCGCTCGCCCTGGAGCCTGCCCTGGCGTCCCCGCGGGCGCCGCCAACTTCTTGGCCATG
A L A L E P A L A S P A G A A N F L A M
GTAGACAACCTGCAGGGGGACTCTGGCCGCGGCTACTACCTGGAGATGCTGATCGGGACC
V D N L Q G D S G R G Y Y L E M L I G T
CCCCCGCAGAAGCTACAGATTCTCGTTGACACTGGAAGCAGTAACTTTGCCGTGGCAGGA
P P Q K L Q I L V D T G S S N F A V A G
ACCCCGCACTCCTACATAGACACGTACTTTGACACAGAGAGGTCTAGCAGATACCGCTCC
T P H S Y I D T Y F D T E R S S T Y R S
AAGGGCTTTGACGTCACAGTGAAGTACACACAAGGAAGCTGGACGGGCTTCGTTGGGGAA
K G F D V T V K Y T Q G S W T G F V G E
GACCTCGTCACCATCCCCAAAGGCTTCAATACTTCTTTTCTTGTCAACATTGCCACTATT
D L V T I P K G F N T S F L V N I A T I
TTTGAATCAGAGAATTTCTTTTTGCCTGGGATTAAATGGAATGGAATACTTGGCCTAGCT
F E S E N F F L P G I K W N G I L G L A
TATGCCACACTTGCCAAGCCATCAAGTTCTCTGCAGACCTTCTTCGACTCCCTGGTGACA
Y A T L A K P S S S L E T F F D S L V T
CAAGCAAACATCCCCAACGTTTTCTCCATGCAGATGTGTGGAGCCGGCTTGCCCGTTGCT
Q A N I P N V F S M Q M C G A G L P V A
GGATCTGGGACCAACGGAGGTAGTCTTGTCTTGGGTGGAATTGAACCAAGTTTGTATAAA
G S G T N G G S L V L G G I E P S L Y K
GGAGACATCTGGTATACCCCTATTAAGGAAGAGTGGTACTACCAGATAGAAATTCTGAAA
G D I W Y T P I K E E W Y Y Q I E I L K
TTGGAAATTGGAGGCCAAAGCCTTAATCTGGACTGCAGAGAGTATAACGCAGACAAGGCC
L E I G G Q S L N L D C R E Y N A D K A
ATCGTGGACAGTGGCACCACGCTGCTGCGCCTGCCCCAGAAGGTGTTTGATGCGGTGGTG
I V D S G T T L L R L P Q K V F D A V V
GAAGCTGTGGCCCGCGCATCTCTGATTCCAGAATTCTCTGATGGTTTCTGGACTGGGTCC
E A V A R A S L I P E F S D G F W T G S
CAGCTGGCGTGCTGGACGAATTCGGAAACACCTTGGTCTTACTTCCCTAAAATCTCCATC
Q L A C W T N S E T P W S Y F P K I S I
TACCTGAGAGATGAGAACTCCAGCAGGTCATTCCGTATCACAATCCTGCCTCAGCTTTAC
Y L R D E N S S R S F R I T I L P Q L Y
ATTCAGCCCATGATGGGGGCCGGCCTGAATTATGAATGCTACCGATTCGGCATTTCCCCA
I Q P M M G A G L N Y E C Y R F G I S P
TCCACAAATGCGCTGGTGATCGGTGCCACGGTGATGGAGGGCTTCTACGTCATCTTCGAC
S T N A L V I G A T V M E G F Y V I F D
AGAGCCCAGAAGAGGGTGGGCTTCGCAGCGAGCCCCTGTGCAGAAATTGCAGGTGCTGCA